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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,060	11/08/1999	James T Kealey	014/002C	6093

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EXAMINER	
GIBBS, TERRA C	
ART UNIT	**PAPER NUMBER**
1635	

MAIL DATE	DELIVERY MODE
05/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/436,060	KEALEY ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *38 and 39* is/are allowed.

6)☒ Claim(s) *34-37,40 and 41* is/are rejected.

7)☒ Claim(s) *42-44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission mailed on February 16, 2007 has been entered.

Claim 34 has been amended. New claim 44 is acknowledged.

Claims 34-44 are pending in the instant application.

Claims 34-44 have been examined on the merits.

Response to Arguments

Applicants Amendment and Response filed February 16, 2007 have been considered. Rejections and/or objections not reiterated from the previous Office Action mailed October 16, 2006 are hereby withdrawn. Any arguments addressing said rejections and/or objections are moot. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 34-36, 40, and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by Villeponteau et al. [U.S. Patent No. 5,776,679, made of record in the previous Office Action mailed December 22, 2004].

Claim 34 is drawn to a pharmaceutical composition, suitable for pharmaceutical use in a mammal, comprising a polynucleotide in a pharmaceutically acceptable carrier, wherein the polynucleotide

(a) has a sequence of at least 7 nucleotides that specifically hybridizes to a first nucleotide sequence within an accessible region of the RNA component of human telomerase ("hTR"), wherein the accessible region is selected from nucleotides 137-196, nucleotide 290-319, and nucleotides 350-380 of hTR (SEQ ID NO:16),

(b) does not hybridize to a second nucleotide sequence within the template region of the hTR, said template region being nucleotide 46-55 of SEQ ID NO:16, and

(c) is effective to inhibit the synthesis of telomeric DNA by telomerase.

Claims 35, 36, 40, and 41 are dependent on claim 34 and include all the limitations of claim 34 with the further limitations wherein said polynucleotide has a sequence of about 10 to about 50 nucleotides that specifically hybridizes to the first nucleic acid

sequence; wherein said polynucleotide has a sequence of about 15 to about 35 nucleotides that specifically hybridizes to the first nucleic acid sequence; and wherein said polynucleotide comprises a sequence of at least 7 nucleotide that specifically hybridizes to a first nucleotide sequence within an accessible region of the RNA component of a human telomerase (hTR), said accessible region being nucleotides 137-196 or nucleotides 137-166 of SEQ ID NO:16.

It is noted that the instant specification at page 9, lines 25-33 recites, "pharmaceutical composition" refers to a composition suitable for pharmaceutical use in a mammal. A pharmaceutical composition comprises a pharmacologically effective amount of an active agent and a pharmaceutically acceptable carrier. "Pharmacologically effective amount" refers to that amount of an agent effective to produce the intended pharmacological result. "Pharmaceutically acceptable carrier" refers to any of the standard pharmaceutical carriers, buffers, and excipients". Given this disclosure, the Examiner is interpreting the term, "pharmaceutical composition" to simply comprise a buffer.

Villeponteau et al. disclose the preparation of antisense plasmids for the RNA component of human telomerase using the following primer:

5'-GTTTGCTCTAGAATGAACGGTGGAAG-3' (see column 35, line 1, at primer R3C, which is 26 nucleotides in length). It is noted that the PCR reaction using primer R3C contained appropriate buffers as described at columns 32 and 33, lines 61-67 and 1-4, respectively. PCR primer R3C is reverse complementary to nucleobases 145-170 SEQ ID NO:16 of the instant invention. It is further noted that the reverse

complimentarity between the PCR primer disclosed by Villeponteau et al. and nucleobases 145-170 of SEQ ID NO:16 is contiguous as it contains no mismatches. Given this high degree of complementarity, the PCR primer disclosed by Villeponteau et al. meets the structural limitations of the claimed invention and would be expected to "specifically hybridize" to the accessible region of nucleotides 137-196 and/or nucleotides 137-166 of SEQ ID NO:16 as claimed since the instant specification at page 10 lines 19 and 20 teaches, "a polynucleotide "specifically hybridizes" to a target polynucleotide if the polynucleotide hybridizes to the target under stringent conditions". It is noted that the instant specification at page 10, lines 20-26 describes "stringent conditions" to be generally, "the temperature and ionic conditions used in nucleic acid hybridization". Accordingly, the PCR primer disclosed by Villeponteau et al. would specifically hybridize to the accessible region of nucleotides 137-196 and/or nucleotides 137-166 of SEQ ID NO:16 as claimed.

The burden of establishing whether the prior art primer disclosed by Villeponteau et al. has the further function of inhibiting the synthesis of telomeric DNA by telomerase as instant claimed falls to Applicant. See (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977): "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product... Whether the rejection is based on 'inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its

fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted]. See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2122 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the PCR primer disclosed by Villeponteau et al. would or would not have the additional functional limitation of inhibiting the synthesis of telomeric DNA by telomerase under generally any assay condition.

Therefore, absent evidence to the contrary, claims 34-36, 40, and 41 are anticipated by Villeponteau et al. [U.S. Patent No. 5,776,679].

Response to Arguments

In Applicant's response to this rejection filed February 16, 2007, Applicants argue that the PCR reaction mixture taught by Villeponteau et al., containing reactive components such as nucleotides (dNTP and radioactilvey labeled dATP), *Taq* polymerase, and T4 gene 32 protein would not be "suitable for pharmaceutical use in a mammal" as defined in the instant claims. Applicants also argue that the primer mixture would not be "pharmacologically effective" in the presence of cDNA to which it is designed to hybridize.

This argument has been fully considered but is not found persuasive. The Examiner agrees that the PCR reaction mixture taught by Villeponteau et al., contains

reactive components such as nucleotides (dNTP and radioactilvey labeled dATP), *Taq* polymerase, and T4 gene 32 protein. However, the issue is that the claims recite, "A pharmaceutical composition, suitable for pharmaceutical use in a mammal, comprising a polynucleotide in a pharmaceutically acceptable carrier", where "comprising" is interpreted as open-ended language. For more explanation, see MPEP 2111.03 where it states, "The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps". Therefore, the claims do not exclude the reactive components such as nucleotides (dNTP and radioactilvey labeled dATP), *Taq* polymerase, and T4 gene 32 protein as taught by Villeponteau et al.

Thus, given the open-ended language of the claims, Villeponteau et al. clearly anticipate claims 34-36, 40, and 41, absent evidence to the contrary.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 34-37, 40, and 41 are rejected under 35 U.S.C. 103(a) as being anticipated by Villeponteau et al. [U.S. Patent No. 5,776,679, made of record in the Office Action mailed December 22, 2004] in view of Nakamaye et al. (Nucleic Acids Research, 1988 Vol. 16:9947-9959).

Claim 34 is drawn to a pharmaceutical composition, suitable for pharmaceutical use in a mammal, comprising a polynucleotide in a pharmaceutically acceptable carrier, wherein the polynucleotide

(a) has a sequence of at least 7 nucleotides that specifically hybridizes to a first nucleotide sequence within an accessible region of the RNA component of human telomerase ("hTR"), wherein the accessible region is selected from nucleotides 137-196, nucleotide 290-319, and nucleotides 350-380 of hTR (SEQ ID NO:16),

(b) does not hybridize to a second nucleotide sequence within the template region of the hTR, said template region being nucleotide 46-55 of SEQ ID NO:16, and

(c) is effective to inhibit the synthesis of telomeric DNA by telomerase.

Claims 35-37, 40 and 41 are dependent on claim 34 and include all the limitations of claim 34 with the further limitations wherein said polynucleotide has a sequence of about 10 to about 50 nucleotides that specifically hybridizes to the first nucleic acid sequence; wherein said polynucleotide has a sequence of about 15 to about 35 nucleotides that specifically hybridizes to the first nucleic acid sequence; wherein said polynucleotide comprises a sequence of at least 7 nucleotide that specifically hybridizes to a first nucleotide sequence within an accessible region of the RNA component of a human telomerase (hTR), said accessible region being nucleotides 137-196 or nucleotides 137-166 of SEQ ID NO:16; and wherein said polynucleotide comprises a nucleotide analog or non-naturally occurring nucleotide linkage selected from phosphorothioates, phosphoramidates, methyl phosphonates, chiral-methyl phosphonates, 2-O-methyl ribonucleotides and peptide-nucleic acids.

It is noted that the instant specification at page 9, lines 25-33 recites, "pharmaceutical composition" refers to a composition suitable for pharmaceutical use in a mammal. A pharmaceutical composition comprises a pharmacologically effective amount of an active agent and a pharmaceutically acceptable carrier. "Pharmacologically effective amount" refers to that amount of an agent effective to produce the intended pharmacological result. "Pharmaceutically acceptable carrier" refers to any of the standard pharmaceutical carriers, buffers, and excipients". Given this disclosure, the Examiner is interpreting the term, "pharmaceutical composition" to simply comprise a buffer.

Villeponteau et al. teach the preparation of antisense plasmids for the RNA component of human telomerase using the following primer:

5'-GTTTGCTCTAGAATGAACGGTGGAAG-3' (see column 35, line 1, at primer R3C, which is 26 nucleotides in length). It is noted that the PCR reaction using primer R3C contained appropriate buffers as described at columns 32 and 33, lines 61-67 and 1-4, respectively. PCR primer R3C is reverse complementary to nucleobases 145-170 SEQ ID NO:16 of the instant invention. It is further noted that the reverse complimentarity between the PCR primer taught by Villeponteau et al. and nucleobases 145-170 of SEQ ID NO:16 is contiguous as it contains no mismatches. Given this high degree of complementarity, the PCR primer taught by Villeponteau et al. meets the structural limitations of the claimed invention and would be expected to "specifically hybridize" to the accessible region of nucleotides 137-196 and/or nucleotides 137-166 of SEQ ID NO:16 as claimed since the instant specification at page 10 lines 19 and 20

teaches, "a polynucleotide "specifically hybridizes" to a target polynucleotide if the polynucleotide hybridizes to the target under stringent conditions". It is noted that the instant specification at page 10, lines 20-26 describes "stringent conditions" to be generally, "the temperature and ionic conditions used in nucleic acid hybridization". Accordingly, the PCR primer taught by Villeponteau et al. would specifically hybridize to the accessible region of nucleotides 137-196 and/or nucleotides 137-166 of SEQ ID NO:16 as claimed.

The burden of establishing whether the prior art primer taught by Villeponteau et al. has the further function of inhibiting the synthesis of telomeric DNA by telomerase as instant claimed falls to Applicant. See (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977): "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product... Whether the rejection is based on 'inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted]. See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2122 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the PCR

primer taught by Villeponteau et al. would or would not have the additional functional limitation of inhibiting the synthesis of telomeric DNA by telomerase under generally any assay condition.

Villeponteau et al. do not teach a pharmaceutical composition comprising a polynucleotide in a pharmaceutically acceptable carrier, wherein the polynucleotide further comprises a non-naturally occurring nucleotide linkage, including a phosphorothioate linkage.

Nakamaye et al. teach an alternative method for direct sequencing of DNA generated by *Taq* polymerase-PCR, via the incorporation of phosphorothioate nucleotides and followed by treatment with an alkylating agents that cleaves specifically at the phosphorothioate positions (see Abstract). Specifically, Nakamaye et al. teach PCR performed using three normal nucleotides and one phosphorothioate-containing nucleotide resulted in a good yield of PCR product (see Figure 1) that could be successfully and directly sequenced (see page 9954).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a polynucleotide comprising a sequence of at least 7 nucleotides that specifically hybridizes to an accessible region of the RNA component of human telomerase (hTR), wherein the accessible region is nucleotides 137-196 or nucleotides 137-166 of SEQ ID NO:16 of the instant invention using the teachings of Villeponteau et al. It would have been obvious to one of ordinary skill in the art to incorporate a phosphorothioate linkage on said polynucleotide using the teachings and motivation of Nakamaye et al.

One of ordinary skill in the art would have been motivated to make a polynucleotide comprising a sequence of at least 7 nucleotides that specifically hybridizes to an accessible region of the RNA component of human telomerase (hTR), wherein the accessible region is nucleotides 137-196 or nucleotides 137-166 of SEQ ID NO:16 of the instant invention since the prior art taught such a polynucleotide could be used as a primer in the preparation of antisense plasmids for the RNA component of human telomerase, which is important in cloning human telomerase cDNA (see Villeponteau et al.). One of ordinary skill in the art would have been motivated to incorporate a phosphorothioate linkage on said polynucleotide since the prior art has taught that phosphorothioate-containing primers yield PCR products that can be directly sequenced (see Nakamaye et al.).

One of ordinary skill in the art would have expected success at making a polynucleotide comprising a sequence of at least 7 nucleotides that specifically hybridizes to an accessible region of the RNA component of human telomerase (hTR), wherein the accessible region is nucleotides 137-196 or nucleotides 137-166 of SEQ ID NO:16 of the instant invention since Villeponteau et al. taught the successful use and design of such a polynucleotide in the preparation of antisense plasmids for the RNA component of human telomerase. One of ordinary skill in the art would have expected success at modifying the polynucleotide to comprise a phosphorothioate linkage since Nakamaye et al. taught the successful use and design of phosphorothioate-containing primers in PCR and DNA sequencing.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Claims 42 and 43 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 42 and 43 are considered free of the prior art since the prior art does not teach or fairly suggest a pharmaceutical composition comprising a polynucleotide in a pharmaceutically acceptable carrier, wherein the polynucleotide

(a) has a sequence of at least 7 nucleotides that specifically hybridizes to a first nucleotide sequence within an accessible region of the RNA component of human telomerase ("hTR"), wherein the accessible region is selected from nucleotides 290-319, and nucleotides 350-380 of hTR (SEQ ID NO:16),

(b) does not hybridize to a second nucleotide sequence within the template region of the hTR, said template region being nucleotide 46-55 of SEQ ID NO:16, and

(c) is effective to inhibit the synthesis of telomeric DNA by telomerase.

Additionally, claim 44 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claim 44 is considered free of the prior art since the prior art does not teach or fairly suggest a pharmaceutical

composition consisting of a polynucleotide in a pharmaceutically acceptable carrier, wherein the polynucleotide

(a) has a sequence of at least 7 nucleotides that specifically hybridizes to a first nucleotide sequence within an accessible region of the RNA component of human telomerase ("hTR"), wherein the accessible region is selected from nucleotides 137-196, 290-319, and nucleotides 350-380 of hTR (SEQ ID NO:16),

(b) does not hybridize to a second nucleotide sequence within the template region of the hTR, said template region being nucleotide 46-55 of SEQ ID NO:16, and

(c) is effective to inhibit the synthesis of telomeric DNA by telomerase.

Allowable Subject Matter

Claims 38 and 39 are allowable. Claims 38 and 39 are considered to be free of the prior art since the prior art does not teach or fairly suggest a polynucleotide consisting of a sequence selected from the group consisting of SEQ ID NOs: 2-14 or pharmaceutical compositions therein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

tcg
April 29, 2007